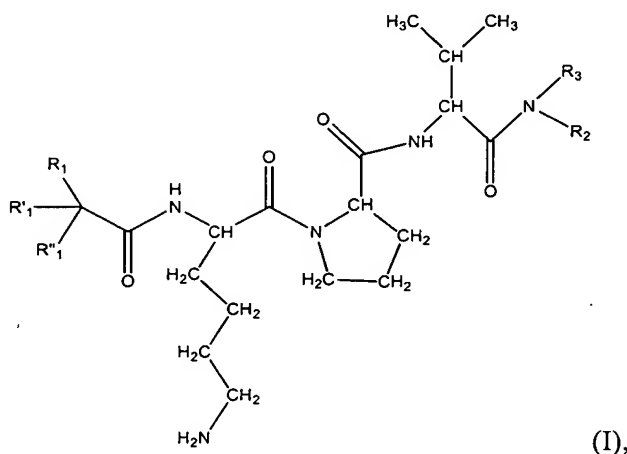


IN THE CLAIMS

1. (currently amended) A ~~solution-synthesis-method~~ synthesis-method for the synthesis of a KPV tripeptide diamide ~~derivate-derivative~~ represented by the following formula (I)



or for a salt thereof, ~~independently from the~~ independent of stereochemistry of the ~~implemented amino-acids~~ wherein:

- a) R_1 , R'_1 and R''_1 represent, independently from each other, a hydrogen atom or
- a linear or branched C_1 - C_{22} alkyl moiety, optionally interrupted by a heteroatom such as O or N or S or Si,
 - C_4 - C_{10} cycloalkyl moiety,
 - a linear or branched C_1 - C_{22} polyfluoroalkyl or perfluoroalkyl moiety,
 - an aryl moiety optionally substituted by one or more halogen atoms such as Cl, F, Br or I or one or more linear or branched C_1 - C_4 alkyl moieties,
 - an aralkyl moiety,
 - or R_1 and R'_1 could form with $C(R''_1)$ a saturated ring with from 3 to 7 atoms, optionally substituted by one or more linear or branched C_1 - C_4 alkyl moieties and/or optionally containing a heteroatom such as O, S or N,

with the proviso that the $R_1(R'_1)(R''_1)CO$ group does not represent an amino acid residue or a peptide-residue;

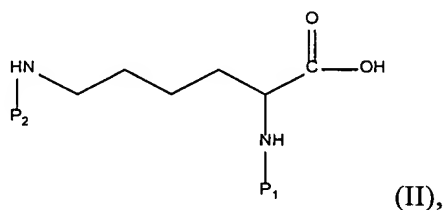
- b) R_2 and R_3 represent, independently from each other, a hydrogen atom or represent
- a linear or branched C_1 - C_{24} alkyl moiety, optionally interrupted by a heteroatom such as O or N or S or Si,

- a C₄-C₁₀ cycloalkyl moiety,
- a linear or branched C₁-C₂₂ polyfluoroalkyl or perfluoroalkyl moiety,
- an aryl moiety optionally substituted by one or more halogen atoms such as Cl, F, Br or I, or one or more linear or branched C₁-C₄ alkyl moieties,
- an aralkyl moiety,
- or R₂ and R₃ could form with the nitrogen atom a saturated ring with from 5 or 6 atoms optionally substituted by one or more linear or branched C₁-C₄ alkyl moieties, said saturated ring optionally containing a heteroatom such as O, S or also an additional nitrogen atom,

with the proviso that the N(R₂) (R₃) group does not represent an amino acid or a peptide residue;

said method comprising:

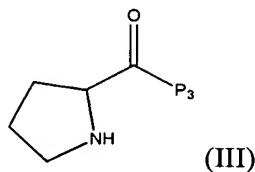
a) reacting a lysine diprotected residue having the following formula (II):



optionally salified by a mineral or organic base,

wherein P₁ and P₂, may be the same or ~~diffient~~ different and each represent independently from one another a protective group,

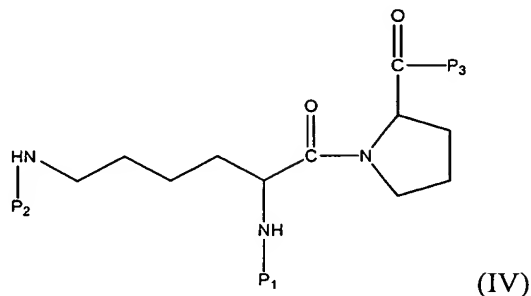
with a Proline residue having the following formula (III):



optionally salified by a mineral or organic acid,

wherein P₃ represents a protective group differing from any of the P₁ and P₂ protective groups, or wherein P₃ represents a hydroxyl group,

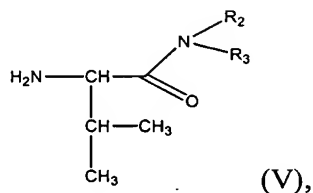
in the presence of an activation reagent or a coupling reagent in a solvent, so as to obtain the following compound having the formula (IV):



wherein P₁, P₂ and P₃ have the above-mentioned meanings,

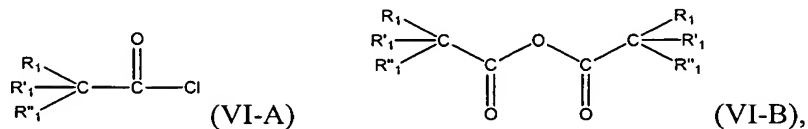
b) and, in any order,

1) coupling a valine compound having the following formula (V) on the C-terminal function of the Proline residue of the compound with formula (IV) ~~wherein~~ when P₃ represents OH,:

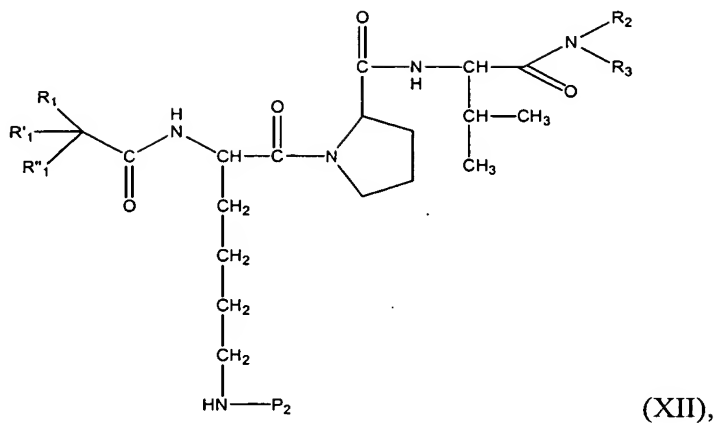


and wherein R₂ and R₃ have the same meanings as hereinabove, and removing the P₁ protective group,

2) amidating the NH₂(α) group in a N-terminal position of the lysine residue by a compound having the following formula (VI-A) or (VI-B):



so as to obtain the following compound having the formula (XII):



wherein P_2 , R_1 , R'_1 , R''_1 , R_2 and R_3 have the same meaning as hereinabove;

c) removing the P₂ protective group from the compound having the formula (XII) so as to obtain the compound having the formula (I), optionally under the form of a mineral or organic salt.

2. (original) The method according to claim 1, wherein the compound having the formula (I) is a salt selected amongst the hydrochlorides, hydrobromides, sulphates, acetates, citrates, tartrates, lactates, phosphates, hydrogenophosphates, propionates and succinates.

3. (original) The method according to claims 1 or 2, wherein the Lysine, Proline or Valine amino acid residues are any of the stereoisomers of such residues.

4. (original) The method according to claims 1 or 2, wherein the salt is obtained during step c) through introducing the corresponding acid.

5. (original) The method according to claim 4, wherein the acid is acetic acid, hydrochloric acid, hydrobromic acid, sulphuric acid, citric acid, tartaric acid, lactic acid, phosphoric acid, hydrogenophosphoric acid, propionic acid or succinic acid.

6. (original) The method according to claim 5, wherein the acid is acetic or hydrochloric acid.

7. (currently amended) The method according to claims 1 or 2, wherein the P₁ and P₂ protective groups represent, independently from each other, Adoc (=1-adamantyloxycarbonyl) BOC (=t-butyloxycarbonyl), 2-bromo-Z (=2-bromo-benzyloxycarbonyl), 2-chloro-Z (=2-chloro-benzyloxycarbonyl), Fmoc (=9-fluorenylmethoxycarbonyl), Formyl, Nicotinoyl, 4-nitro-Z (=4-nitro-benzyloxycarbonyl), Tfa (=trifluoroacetyl), Tos (=p-toluenesulfonyl), Z(=benzyloxycarbonyl) or Adpoc (=1-(adamantyl)-1-methylethoxycarbonyl).

8. (currently amended) The method according to claims 1 or 2, wherein the P₁ and P₂ protective groups are selected such as to be removed respectively ~~in~~under distinct operating conditions.

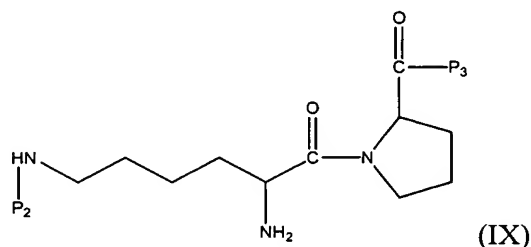
9. (currently amended) The method according to claims 1 or 2, wherein the compound having the formula (II) is salified by an organic base, ~~preferably an organic amine~~.

10. (original) The method according to claims 1 or 2, wherein the compound having the formula (III) is salified by a mineral or an organic acid.

11. (currently amended) A method according to claims 1 or 2, wherein in step a), the peptide coupling reaction occurs in the presence of an activation or a coupling reagent selected amongst carbodiimides, water-soluble carbodiimides, phosphonium salts, PyBOP (= (benzotriazol-1-yloxy)tripyrrolidino-phosphonium hexafluorophosphate), PyBROP (= bromotripyrrolidino-phosphonium hexafluorophosphate), PyCloP (= chlorotripyrrolidino-phosphonium hexafluorophosphate), or also by means of reagents ~~selected amongst~~selected amongst PyClU (= chloro-N,N,N',N'-bis(tetramethylene)formamidinium hexafluoro-phosphate), N-hydroxysuccinimide, EEDQ (= 1-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinolin), CDI (= carbonyldiimidazole), or chloroformates

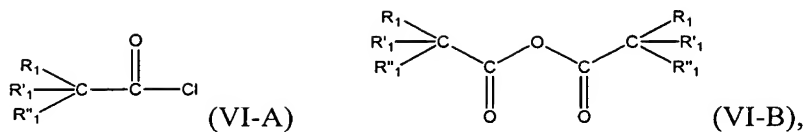
12. (currently amended) The method according to claims 1 or 2, wherein the step b) further comprises the following steps :

b1) removing the P₁ protective group of the compound with formula (IV) wherein P₃ represents a protective group, so as to obtain the compound with formula (IX):

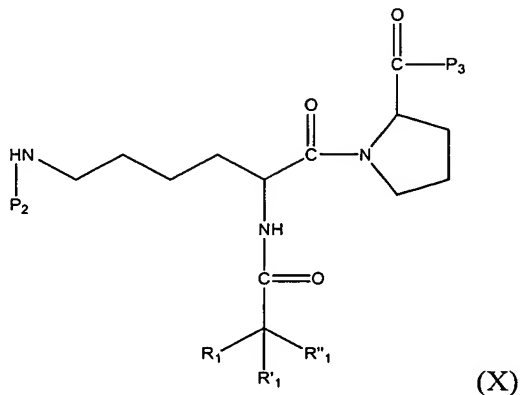


wherein P₁ has the same meaning as in claim 1 ~~and P₃ represents a protective group~~;

b2) amidating the NH₂(α) group of the lysine residue of the compound having the formula (IX) with the following compound having the formula (VI-A) or the compound having the formula (VI-B):

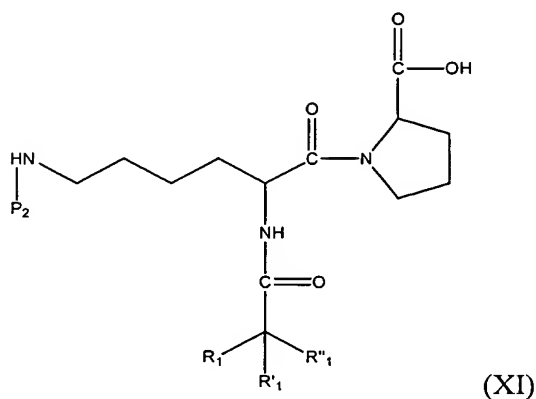


wherein R_1 , R'_1 and R''_1 have the same meanings as in claim 1, so as to obtain the following compound with formula (X);



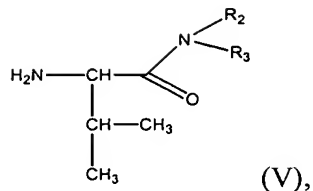
wherein R_1 , R'_1 , R''_1 , P_2 have the same meaning as in claim 1 and P_3 represents a protective group;

b3) Removing the P_3 protective group from the compound having formula (X) so as to obtain the compound with formula (XI):

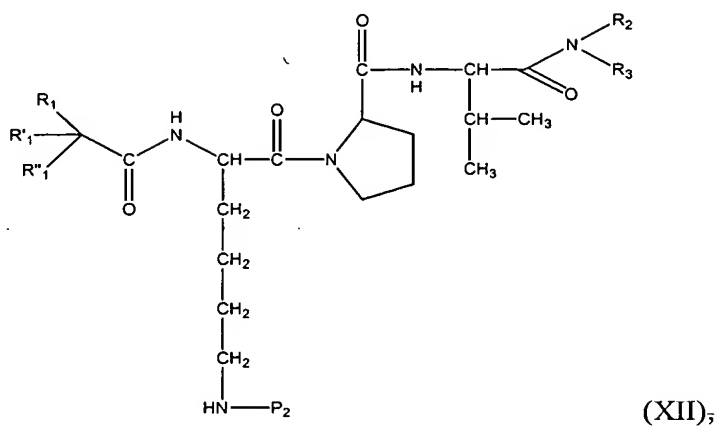


wherein R_1 , R'_1 , R''_1 and P_2 have the same meaning as in claim 1;

b4) coupling the compound having formula (XI) with the valine compound having the following formula (V), optionally salified by a mineral or organic acid:



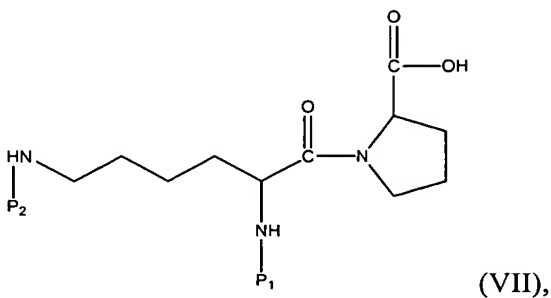
wherein R_2 and R_3 have the same meaning as hereinabove, so as to obtain the following compound having formula (XII):



wherein P_2 , R_1 , R'_1 , R''_1 , R_2 and R_3 have the same meanings as hereinabove

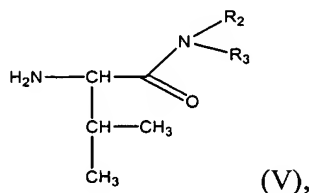
13. (currently amended) The method according to claims 1 or 2, wherein the step b) further comprises the following steps :

b5) removing group P_3 from the compound having formula (IV) where the P_3 group represents a protective group, so as to obtain the compound with the following formula (VII):

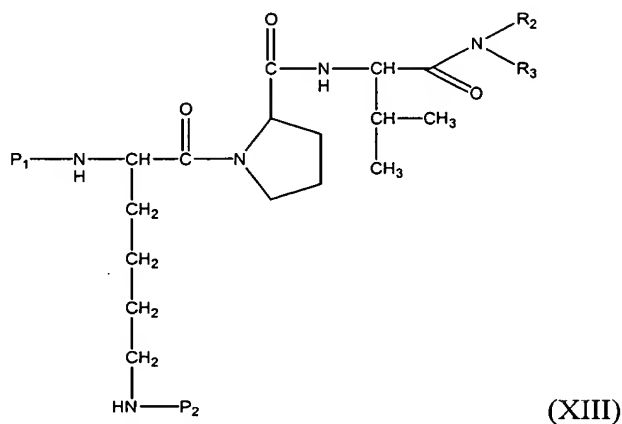


wherein P_1 and P_2 have the same meanings as in claim 2;

b6) coupling the compound having formula (VII) with the valine compound having the formula (V), optionally salified by a mineral or an organic acid:

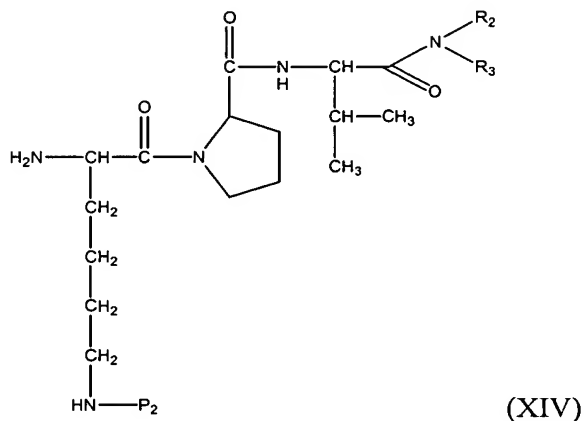


wherein R_2 and R_3 have the same meaning as in claim 1 so as to obtain a compound having formula (XIII):



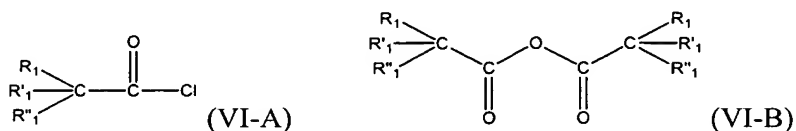
wherein P_1 , P_2 , R_2 and R_3 have the same meaning as hereinabove ;

b7) removing the P_1 protective group from the compound having the formula (XIII) so as to obtain the following compound having the formula (XIV), and optionally salified by a mineral or an organic acid:

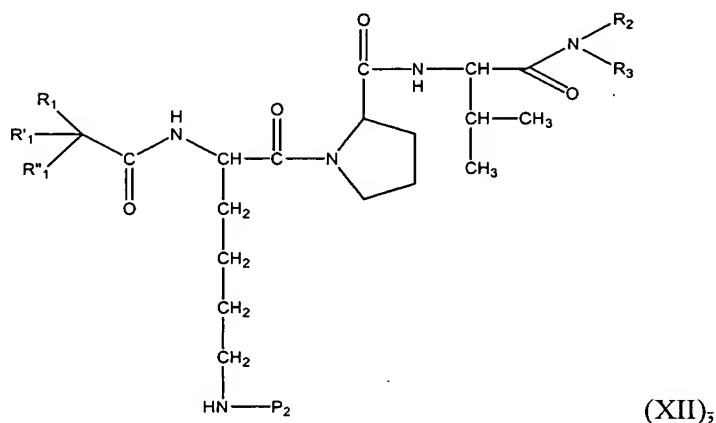


~~wherein P_2 , R_2 and R_3 have the same meaning as hereinabove;~~

b8) amidating the $NH_2(\alpha)$ group of the lysine residue of the compound having the formula (XIV) with the compound having the formula (VI-A) or the following compound having the formula (VI-B), optionally mineralized by a mineral or an organic acid:



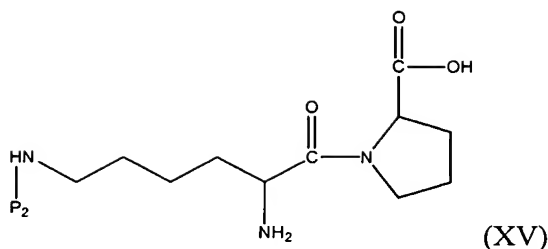
wherein R_1 , R'_1 et R''_1 have the same meanings as in claim 1, so as to obtain the following compound having the formula (XII):



~~wherein P_2 , R_1 , R'_1 , R''_1 , R_2 and R_3 have the same meanings as hereinabove~~

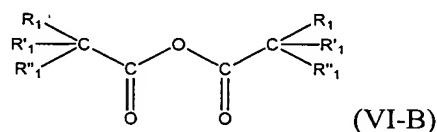
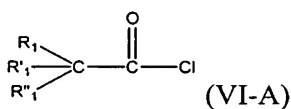
14. (currently amended) The method according to claims 1 or 2, ~~wherein~~instepwherein
step b) further comprises the following steps :

b9) removing the P_1 protective group from the compound having the formula (VII) wherein the P_3 group represents a hydroxy group, so as to obtain the following compound having the formula (XV):



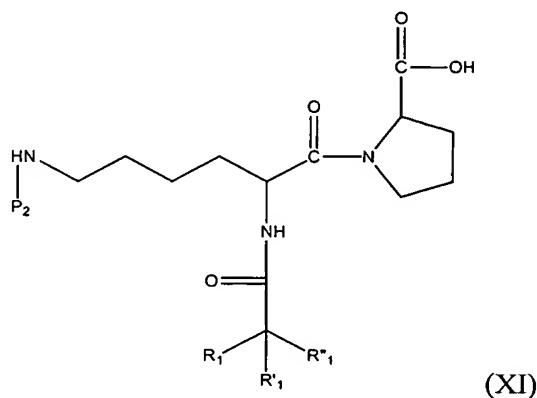
wherein P_2 has the same meaning as in claim 2;

b10) amidating the $NH_2(\alpha)$ group of the lysine residue of the compound having the formula (XV) with the compound having the formula (VI-A) or the following compound having the formula (VI-B):



wherein R_1 , R'_1 et R''_1 have the same meanings as in claim 1,

so as to obtain the following compound (XI), optionally salified by an organic or a mineral base:



wherein P_2 , R_1 , R'_1 et R''_1 have the same meaning as hereinabove ;

b11) coupling the compound having the formula (XI) with the valine following compound having the formula (V), optionally salified by a mineral or an organic acid:



wherein R₂ ~~et~~-and R₃ have the same meanings as in claim 1; so as to obtain the compound of the formula (XII):



wherein P_2 , R_1 , R'_1 , R''_1 , R_2 and R_3 have the same meaning as hereinabove

15. (original) The method according to claims 1 or 2, wherein in the compound having the formula (II), the P₁ protective group is t-butyloxycarbonyl (BOC) and the P₂ protective group is benzyloxycarbonyl (Z).

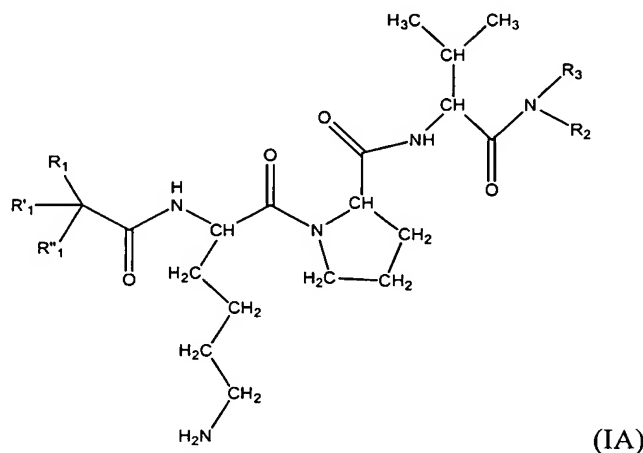
16. (original) The method according to claims 1 or 2, wherein in the compound of the formula (III), the P₃ protective group is the OBzl benzyl ester group.

17. (currently amended) The method according to claims 1 or 2, wherein in the compound having the formula (I), the R₁, R'₁ and R''₁ group-groups represent each a hydrogen atom.

18. (original) The method according to claims 1 or 2, wherein in the compound having the formula (I), the R₂ and R₃ groups represent each a hydrogenatom.

19. (original) The method according to claims 1 or 2, wherein the P₁ protective group is t-butyloxycarbonyl (BOC), the P₂ protective group is benzyloxycarbonyl (Z) and the P₃ protective group is OBzl benzyl ester.

20. (currently amended) A KPV tripeptide diamide ~~derivate~~derivative or salt thereof represented by the following formula (IA):



wherein:

- a) R_1 , R'_1 and R''_1 represent, independently from each other, a hydrogen atom or
- a linear or branched C_1 - C_{22} alkyl moiety, optionally interrupted by a heteroatom such as O or N or S or Si,
 - C_4 - C_{10} cycloalkyl moiety,
 - a linear or branched C_1 - C_{22} polyfluoroalkyl or perfluoroalkyl moiety,
 - an aryl moiety optionally substituted by one or more halogen atoms such as Cl, F, Br or I or one or more linear or branched C_1 - C_4 alkyl moieties,
 - an aralkyl moiety,
 - or R_1 and R'_1 could form with $C(R''_1)$ a saturated ring with from 3 to 7 atoms, optionally substituted by one or more linear or branched C_1 - C_4 alkyl moieties and/or optionally containing a heteroatom such as O, S or N,
 - hydrogen,
- with the proviso that the $R_1(R'_1)(R''_1)CO$ group does not represent an amino acid residue or a peptide residue with at least one of R_1 , R'_1 , R''_1 being different from hydrogen.
- b) R_2 and R_3 represent, independently from each other, a hydrogen atom or represent
- a linear or branched C_1 - C_{24} alkyl moiety, optionally interrupted by a heteroatom such as O or N or S or Si,
 - a C_4 - C_{10} cycloalkyl moiety,

- a linear or branched C₁-C₂₂ polyfluoroalkyl or perfluoroalkyl moiety,
- an aryl moiety optionally substituted by one or more halogen atoms such as Cl, F, Br or I, or one or more linear or branched C₁-C₄ alkyl moieties,
- an aralkyl moiety,
- or R₂ and R₃ could form with the nitrogen atom a saturated ring with from 5 or 6 atoms optionally substituted by one or more linear or branched C₁-C₄ alkyl moieties, said saturated ring optionally containing a heteroatom such as O, S or also an additional nitrogen atom, with at least one of the residues R₂ or R₃ being different from hydrogen,

with the proviso that the N(R₂) (R₃) group does not represent an amino acid or a peptide residue.

21. (original) The KPV tripeptide diamide derivative according to claim 20, wherein the salt is selected amongst hydrochlorides, hydrobromides, sulphates, acetates, citrates, tartrates, lactates, phosphates, hydrogenophosphates, propionates and succinates.

22. (original) The KPV tripeptide diamide derivate according to claims 20 or 21, wherein the Lysine, Proline or Valine amino acid residues are any of the stereoisomers of each of such residues.

23. (original) A composition comprising: a KPV tripeptide diamide derivative or salt thereof according to claims 20 or 21 in a physiologically acceptable medium.

24. (currently amended) The composition according to claim 23, wherein the physiologically acceptable medium is a cosmetic medium and the KPV ~~tripeptide~~tripeptide diamide derivate or salt thereof is present in an amount ranging from 10⁸ to 10⁻³ g/100g.

25. (currently amended) The composition according to claim 23, wherein the physiologically acceptable medium is a pharmaceutical medium and the KPV ~~tripeptide~~tripeptide diamide derivate is present in an amount greater than 5.10⁻⁴ g/100g.

26. (canceled)

27. (original) The method according to claim 9, wherein the organic base is an organic amine.

28. (original) The method according to claim 1, further comprising the step of deprotecting P3 prior to coupling said valine compound of Formula (V) to said compound of Formula (IV).

29. (original) A method of treating dry or sensitive skin comprising: obtaining a quantity of a composition of claim 23 and applying said composition to the dry or sensitive skin of a patient.

30. (original) A method of treating dry or sensitive skin comprising: obtaining a quantity of a composition of claim 24 and applying said composition to the dry or sensitive skin of a patient.

31. (original) A method of treating dry or sensitive skin comprising: obtaining a quantity of a composition of claim 25 and applying said composition to the dry or sensitive skin of a patient.

32. (new) The method of claim 1 wherein R_1 , R'_1 or R''_1 are a linear or branched C_1 - C_{22} alkyl moiety interrupted by a heteroatom, said heteroatom is selected from O, N, S or Si.

33. (new) The method of claim 1 wherein when R_1 and R'_1 form with $C(R''_1)$ a saturated ring containing a heteroatom, said heteroatom is O, S or N.

34. (new) The method of claim 1 wherein when R_2 and R_3 is a linear or branched C_1 - C_{22} alkyl moiety interrupted by a heteroatom, said heteroatom is selected from O, N, S or Si.

35. (new) The method of claim 1 wherein when R_2 and R_3 form with a nitrogen atom a saturated ring containing a heteroatom, said heteroatom is O, S or N.

36. (new) The method of claim 9 wherein said organic base is an organic amine.

37. (new) The method of claim 1 wherein when R_1 , R'_1 or R''_1 are an aryl moiety optionally substituted by one or more halogen atoms, such halogen is Cl, F, Br or I.

38. (new) The method of claim 1 wherein when R_2 and R_3 form an aryl moiety optionally substituted by one or more halogen atoms, such halogen is Cl, F, Br or I.

39. (new) The KPV tripeptide diamide derivative or salt thereof of claim 20 wherein, when R_1 , R'_1 and R''_1 represent a linear or branched C_1 - C_{22} alkyl moiety interrupted by a heteroatom, said heteroatom is O, N, S or Si.

40. (new) The KPV tripeptide diamide derivative or salt thereof of claim 20 wherein, when R_1 , R'_1 and R''_1 represent an aryl moiety optionally substituted by one or more halogen atoms, such halogen is Cl, F, Br or I.

41. (new) The KPV tripeptide diamide derivative or salt thereof of claim 20 wherein, when R_1 and R'_1 form with $C(R''_1)$ a saturated ring containing a heteroatom, said heteroatom is O, S or N.

42. (new) The KPV tripeptide diamide derivative or salt thereof of claim 20 wherein, when R_2 and R_3 represent a linear or branched C_1 - C_{22} alkyl moiety interrupted by a heteroatom, said heteroatom is O, N, S or Si.

43. (new) The KPV tripeptide diamide derivative or salt thereof of claim 20 wherein, when R_2 and R_3 represent an aryl moiety optionally substituted by one or more halogen atoms, such halogen is Cl, F, Br or I.

44. (new) The KPV tripeptide diamide derivative or salt thereof of claim 20 wherein, when R_2 and R_3 form with a nitrogen atom a saturated ring containing a heteroatom, said heteroatom is O, S or N.

45. (new) A method of making a composition useful for treating dry or sensitive skin comprising obtaining a quantity of a KPV tripeptide diamide derivative or salt thereof as claimed in claim 20 and mixing same in a physiologically acceptable medium so as to produce a dermatological composition.